addition, Claims 1-3 are alleged to be indefinite because the claims contain information in parenthesis.

Applicants have cancelled Claims 1-23 and replaced them with new claims 24-57 which more particularly point out and distinctly claim the subject matter which applicant regards as the invention. The new claims have been added to address each of the rejections cited by the Examiner. In view of the foregoing amendments to the claims, the rejections under 35 U.S.C. §112, second paragraph, should be withdrawn.

2. The Claims Are Not Anticipated Under 35 U.S.C. § 102(b)

Claims 1-3 are rejected under 35 U.S.C. § 102(b) as anticipated by Bottini et al. (1996, European J. of Immunology 26:1816-1824; "Bottini"). The Examiner alleges that Bottini teaches an *in vitro* method of determining the repertoire of NKR immunoreceptors comprising the KIR p58 and the KAR p50 target receptors. According to the Examiner, Bottini teaches an *in vitro* method characterized in that at lest one of the 3' and 5' oligonucleotide pair hybridizes to the target receptor only. Further, the Examiner maintains that Bottini teaches an *in vitro* method characterized in that the 5' oligonucleotide of the 3' and 5' oligonucleotide pair used for an NKR target receptor hybridizes to the DNA or to the cDNA of an NKR receptor counterpart (Figure 8 of Bottini).

Invalidity for anticipation requires that all of the elements and limitations of the claim be found within a single prior art reference. There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of

ordinary skill in the field of the invention. Scripps *Clinic Research & Foundation v. Genentech Inc.*, 927 F.2d 1585, 18 U.S.P.Q. 2d 1001 (Fed. Cir. 1991).

In the present instance, the question is whether Bottini teaches methods for amplification of the particular target immunoreceptors specified in the claims, i.e., the p58.1, p58.2, p70.INH, p140.INH, NKG2A, NKG2B, 50.1, 50.2, p70.ACT, p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F receptors. Clearly the answer to this question is no.

Bottini discloses the identification of a novel p50 NK receptor referred to as pKKA3. As indicated by the amino acid sequences presented in Figure 10, pKKA3 is different from the amino acid sequences of the p58.1, p58.2, p50.1 and p50.2 NK receptors. As set forth in Bottini, the PAX mAb specifically recognize the NK receptor referred to as the pKKA.3 immunoreceptor while the EB6 antibody recognizes the p58.1 and p50.1 receptor and the GL183 antibody recognizes the p58.2 and p50.2 receptor. The PCR amplification demonstrated in Figure 8 of Bottini represents amplification using cDNA derived from a PAX^{+} $EB6^{-}GL183^{-}$ NK cloned cell line. However, since the cell line from which the cDNA was derived lacks EB6 and GL183 reactivity, the amplification depicted in Figure 8 cannot be amplification of the p50.1, p50.2 p58.1 or p58.2. Therefore, Bottini fails to disclose pairs of oligonucleotide primers that may be used to selectively amplified the target NKR immunoreceptors encompassed by Applicant's claims.

Thus, given the differences between the presently claimed invention and the disclosure of Bottini, the invention cannot be anticipated.

3. The Claims Are Not Anticipated Under 35 U.S.C. § 102(a)

Claims 1-3 are rejected under 35 U.S.C. § 102(a) as being anticipated by Hiby et al. (1997, Molecular Immunology, 34:419-430; "Hiby"). The Examiner alleges that Hiby teaches an *in vitro* method of documenting a repertoire of NKR immunoreceptors comprising the KIR p58 and KAR p50 target receptors.

As indicated above, anticipation requires that all the elements and limitations of the claim be found within a single prior art reference. Scripps, *supra*.

A review of Hiby indicates that Hiby merely discloses that human uterine NK cells have a similar repertoire of KIR and KAR receptors expressed on their surface as those found in blood. The study was conducted using RT-PCR and sequencing. The primers utilized in the study, as depicted in Figure 1 and Table 1, were capable of amplifying all KIR and KAR receptors based on sequences conserved between the different types of receptors. While the selected primers were capable of distinguishing between receptors with two Ig-SF extracellular domains versus those with three Ig-SF domains, Hiby fails to disclose pairs of oligonucleotide primers that could be used to selectively amplify specific target receptors. Indeed, the present invention is based on Appplicant's discovery for the first time of oligonucleotide primers capable of selective amplification of a target receptor, *i.e.*, p58.1, p58.2, p70.INH, p140.INH, NKG 2A, NKG 2B, p50.1, p50.2, p70.ACT, p140.ACT, NKG 2C, NKG 20, NKG 2E and NKG 2F.

It is important to note that in the present invention mere detection of hybridization between a nucleic acid encoding an NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair, due to their unique specificity, results in identification of a target receptor. In contrast, Hiby requires sequencing of the amplified fragments to

identify the receptor. Thus, the data presented in Table 3 is derived from sequencing of the amplified fragments.

Given the differences between Hiby and the present invention, Applicants respectfully request withdrawal of the 102(a) rejection.

Entry of the foregoing amendments and remarks into the file of the above identified application is respectfully requested. The Applicants believe that the invention described and defined by the amended claims is patentable over the rejections of the Examiner. Withdrawal of all rejections and reconsideration of the new claims is requested. An early allowance is earnestly sought.

Respectfully submitted,

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APPENDIX A

--24. (New) An *in vitro* method for identifying the repertoire of NKR inhibitory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B receptors, these immunoreceptors being designated hereinafter target receptors, comprising:

(i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, the 3' and 5' oligonucleotides of the same said pair both being capable of hybridization in a buffer comprising 20 mM Tris-HC1, pH 8.4; 50 mM KCl; 2.5 mM $MgCl_2$ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but not hybridizing, under the same hybridization conditions, with a NKR activatory immunoreceptor counterpart and;

(ii) detecting hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR inhibitory receptors.

25. (New) An *in vitro* method for identifying the repertoire of NKR activatory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p50.1, p50.2, p70.ACT. p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F, these immunoreceptors being designated hereinafter target receptors, comprising:

(i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, the 3' and 5' oligonucleotides of the same said pair both being capable of hybridization in a buffer comprising 20 mM Tris-HC1, pH 8.4; 50 mM KCl; 2.5 mM $MgCl_2$ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but not hybridizing, under the same hybridization conditions, with a NKR inhibitory immunoreceptor counterpart:and;

(ii) detecting hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR activatory receptors.

26. (New) The method of claim 24 or 25 wherein the 3' or 5' oligonucleotides are coupled to a marker, allowing detection of hybridization between the nucleic acid sample and the 3' and 5' oligonucleotides.

27. (New) The method of claim 24 or 25 wherein the marker is a fluorescence marker.

28. (New) The method of claim 24 or 25 wherein the marker is a radioactive marker.

29. (New) The method of claim 24 or 25 wherein the 3' and 5' oligonucleotide pair(s) serve(s) as 3' and 5' primers, respectively, for extension by DNA polymerase.

30. (New) The method of claim 24 or 25 wherein hybridization between the nucleic acid sample and the 3' and 5' oligonucleotide pair is detected by PCR amplification.

31. (New) The method of claim 24 or 25 wherein amplification is by nested PCR.

32. (New) The method of claim 24 or 25 wherein the hybridization which may be formed comprises, in addition, the resolution, on a polyacrylamide gel, of the reaction mixture derived from the bringing into contact, as well as the visualization of the presence or of the absence of electrophoretic bands containing the said hybrids which may be formed.

33. (New) The method of claim 24 wherein said method is used to document the genotypic repertoire of KIR immunoreceptors.

34. (New) The method of claim 24 wherein said method is used to document the expression repertoire of KIR immunoreceptors.

35. (new) The method of claim 25 wherein said method is used to document the genotypic repertoire of KAR immunoreceptors.

36. (New) The method of claim 25 wherein said method is used to document the expression repertoire of KAR immunoreceptors.

37. (New) The method of claim 24 or 25 wherein the nucleic acid sample is of human or animal origin.

38. (New) The method of claim 24 or 25 wherein the nucleic acid sample is derived from blood, bone marrow, lymphocytes, NK and/or T cells or transgenic cells.

39. (New) The method of claim 24 or 25 wherein the nucleic acid sample is a genomic or cDNA library.

40. (New) The method of claim 25 wherein the 3' oligonucleotide of a said 3' and 5' oligonucleotide pair, used for determining the repertoire of NKR activatory immunoreceptors, is capable, under the same said hybridization conditions, of hybridizing to a nucleic acid encoding KAR target receptor wherein said nucleic acid encodes the amino acid sequence Lys Ile Pro Phe Thr Ile (K I P F T I) or Lys Leu Pro Phe Thr Ile (K L P F T I) (SEQ ID No. 26 or 27)

41. (New) The method of claim 24 wherein the 5' oligonucleotide comprises the sequence of SEQ ID No. 1, and at least one 3' oligonucleotide selected from the group of 3' oligonucleotides comprising the sequence of SEQ ID No. 5, No. 2, No. 6 or No. 7.

42. (New) The method of claim 24 wherein the 5' oligonucleotide comprises the sequence of SEQ ID No. 4 and at least one 3' oligonucleotide selected from the group of 3' oligonucleotide comprising the sequence of SEQ ID No. 5, No. 2, No. o or No. 7, or a sequence which is derived therefrom.

43. (New) The method of claim 24 wherein a 5' oligonucleotide comprises the sequence of SEQ ID No. 9, or a sequence which is derived therefrom, and at least one 3' oligonucleotide selected from the group of 3' oligonucleotides comprising the sequence SEQ ID No. 5, No. 2, No. 6 or No. 7, or a sequence which is derived therefrom.

44. (New) The method of claim 24 wherein at least one 5' oligonucleotide comprises the sequence of SEQ ID No. 10, No. 11, No. 12 or No. 13 is selected from the group consisting of a 3' oligonucleotide comprising the sequence SEQ ID No. 14, or a sequence which is derived therefrom.

45. (New) The method of claim 25 wherein the 5' oligonucleotide comprises the sequence of SEQ ID No. 1 and a 3' oligonucleotide comprising the sequence of SEQ ID No. 3.

46. (New) The method of claim 25 wherein the 5' oligonucleotide comprises the sequence of SEQ ID No. 8 and a 3' oligonucleotide comprising the sequence of SEQ ID No. 3.

47. (New) The method of claim 25 wherein the 5' oligonucleotide comprising the sequence of SEQ ID No. 9 and a 3' oligonucleotide comprising the sequence SEQ ID No. 3.

48. (New) The method of claim 25 wherein a 5' oligonucleotide comprises the sequence of SEQ ID No. 15 and a 3' oligonucleotide comprising the sequence SEQ ID No.13.

49. (new) The method of claim 24 or 25 wherein the 3' and 5' of oligonucleotide pair(s) have as a target receptor a NKG2 receptor wherein said 3' and 5' oligonucleotide pairs are selected from the group consisting of:

a 5' oligonucleotide comprising the sequence of SEQ ID No. 16 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17;

a 5' oligonucleotide comprising the sequence of SEQ ID No. 18 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17;

a 5' oligonucleotide comprising the sequence of SEQ ID No. 19 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17; and

a 5' oligonucleotide comprising the sequence of SEQ ID No. 20 and a 3' oligonucleotide comprising the sequence SEQ ID No. 21.

50. (New) The method of claim 24 or 25 wherein said method is used to predict or to monitor the acceptance or rejection, by a subject, of cells, tissue or organ which are genetically different.

51. (New) The method according to claim 24 or 25 wherein said method is used to predict or to monitor the safety or the pathogenicity (GVH), for a subject, of a graft or transplant, of cells, tissue or organ which are genetically different.

52. (New) The method according to claim 24 or 25 wherein said method is used to predict or to monitor for a subject of a GVL-type effect on the part of cells, tissue or organ which are genetically different.

53. (New) The method of claim 24 or 25 wherein said method can be used to determine the state of activation of NK and/or T cells within a subject.

54. (New) The method of claim 24 or 25 wherein said method is used to predict or monitor the state of resistance of a subject to infection, wherein said infection is viral, such as an HIV infection, or a parasitic infection, such as malaria, or a bacterial infection, towards autoimmune disease, such as rheumatoid arthritis, or alternatively towards the development of malignant cells such as leukemia cells.

55. (New) The method of claim 24 or 25 wherein said method is used to screen for compositions which can be used to reduce the symptoms associated with infectious autoimmune or proliferation disorders.

56. (New) A kit for carrying out the method of claim 24 or 25 comprising a container, at least one said 3' and 5' oligonucleotide paid, and reagents for carrying out the said method.

57. (New) The kit of claim 56 wherein said 3' and 5' oligonucleotide pair is coupled to a marker.--